



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Preterm birth time trends in Europe

Citation for published version:

Zeitlin, J, Szamotulska, K, Drewniak, N, Mohangoo, AD, Chalmers, J, Sakkeus, L, Irgens, L, Gatt, M, Gissler, M, Blondel, B & Euro-Peristat Preterm Study Group 2013, 'Preterm birth time trends in Europe: a study of 19 countries' BJOG: An International Journal of Obstetrics and Gynaecology, vol. 120, no. 11, pp. 1356-65. DOI: 10.1111/1471-0528.12281

Digital Object Identifier (DOI):

[10.1111/1471-0528.12281](https://doi.org/10.1111/1471-0528.12281)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Publisher's PDF, also known as Version of record

Published In:

BJOG: An International Journal of Obstetrics and Gynaecology

Publisher Rights Statement:

© 2013 The Authors. BJOG: An International Journal of Obstetrics & Gynaecology published by John Wiley and Sons on behalf of the Royal College of Obstetricians and Gynaecologists

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Preterm birth time trends in Europe: a study of 19 countries

J Zeitlin,^{a,b} K Szamotulska,^c N Drewniak,^{a,b} AD Mohangoo,^d J Chalmers,^e L Sakkeus,^f L Irgens,^{g,h} M Gatt,ⁱ M Gissler,^{j,k} B Blondel,^{a,b} The Euro-Peristat Preterm Study Group*

^a INSERM, UMRS 953, Epidemiological Research Unit on Perinatal and Women's and Children's Health, Paris, France ^b UPMC, Paris, France ^c Department of Epidemiology, National Research Institute of Mother and Child, Warsaw, Poland ^d Department Child Health, TNO Netherlands Organization for Applied Scientific Research, Leiden, the Netherlands ^e Information Services Division, NHS National Services Scotland, Edinburgh, UK ^f Estonian Institute for Population Studies, Tallinn University, Tallinn, Estonia ^g Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway ^h Medical Birth Registry of Norway, Norwegian Institute of Public Health, Bergen, Norway ⁱ Department of Health Information and Research, National Obstetric Information Systems (NOIS) Register, G'Mangia, Malta ^j Department of Information, THL National Institute for Health and Welfare, Helsinki, Finland ^k Nordic School of Public Health, Gothenburg, Sweden

Correspondence: J Zeitlin, INSERM, UMRS 953, Epidemiological Research Unit on Perinatal and Women's and Children's Health, 53 avenue de l'Observatoire, 75014 Paris, France. Email jennifer.zeitlin@inserm.fr

Accepted 17 April 2013. Published Online 24 May 2013.

Objective To investigate time trends in preterm birth in Europe by multiplicity, gestational age, and onset of delivery.

Design Analysis of aggregate data from routine sources.

Setting Nineteen European countries.

Population Live births in 1996, 2000, 2004, and 2008.

Methods Annual risk ratios of preterm birth in each country were estimated with year as a continuous variable for all births and by subgroup using log-binomial regression models.

Main outcome measures Overall preterm birth rate and rate by multiplicity, gestational age group, and spontaneous versus non-spontaneous (induced or prelabour caesarean section) onset of labour.

Results Preterm birth rates rose in most countries, but the magnitude of these increases varied. Rises in the multiple birth rate as well as in the preterm birth rate for multiple births

contributed to increases in the overall preterm birth rate. About half of countries experienced no change or decreases in the rates of singleton preterm birth. Where preterm birth rates rose, increases were no more prominent at 35–36 weeks of gestation than at 32–34 weeks of gestation. Variable trends were observed for spontaneous and non-spontaneous preterm births in the 13 countries with mode of onset data; increases were not solely attributed to non-spontaneous preterm births.

Conclusions There was a wide variation in preterm birth trends in European countries. Many countries maintained or reduced rates of singleton preterm birth over the past 15 years, challenging a widespread belief that rising rates are the norm. Understanding these cross-country differences could inform strategies for the prevention of preterm birth.

Keywords Europe, indicated preterm births, multiple births, preterm births, time trends.

Please cite this paper as: Zeitlin J, Szamotulska K, Drewniak N, Mohangoo A, Chalmers J, Sakkeus L, Irgens L, Gatt M, Gissler M, Blondel B. Preterm birth time trends in Europe: a study of 19 countries. BJOG 2013;120:1356–1365.

Introduction

Infants born preterm, defined as births at <37 completed weeks of gestation, are at higher risk of mortality, morbidity, and impaired motor and cognitive development in child-

hood than infants born at term. In high-income countries, between two-thirds and three-quarters of neonatal deaths occur in the 6–11% of infants born alive before 37 weeks of gestation.¹ Infants born before 32 weeks of gestation are at particularly high risk of adverse outcomes, with rates of infant mortality at 10–15% and of cerebral palsy at 5–10%,^{2,3} but moderate preterm birth (at 32–36 weeks of gestation) is also associated with poor outcomes at birth and in childhood.^{4–6} Being born preterm predisposes infants to higher risks of chronic diseases and mortality later in life.^{7,8}

Many countries have reported increased preterm birth rates over the past two decades,^{9–15} and this general trend

*Euro-Peristat Preterm Study Group: C Vutuc (Austria); E Martens (Flanders); P Velebil (Czech Republic); L Sakkeus (Estonia); M Gissler (Finland); B Blondel (France); N Lack, B Misselwitz, P Wenzlaff (Germany); S Bonham (Ireland); J Jaseliuniene (Lithuania); M Gatt (Malta); A Mohangoo, J Nijhuis (the Netherlands); L Irgens, K Klungsoyr (Norway); K Szamotulska (Poland); H Barros (Portugal); Z Novak (Slovenia); F Bolumar (Spain); K Gottvall (Sweden); James Chalmers (UK).

was recently confirmed by a WHO global survey.¹⁶ There are many reasons to expect preterm birth rates to rise. One reason is increasing multiple pregnancy rates, associated with the use of subfertility treatments and later maternal age at childbirth.^{17,18} The preterm birth rate for multiples is 40–60%, compared with 5–10% for singletons.¹⁹ Second, the survival of very preterm infants has improved markedly over recent decades because of medical advances in neonatal care, such as antenatal corticosteroids and surfactants,²⁰ and their improved prognosis has changed perceptions of the risk associated with prematurity versus other pregnancy complications. This has lowered the threshold for indicated (alternatively termed non-spontaneous or provider-initiated) preterm births, and has led to the rise in number of these births.^{21–23} Other risk factors for spontaneous and non-spontaneous preterm birth, such as *in vitro* fertilisation (IVF), older maternal age, and higher maternal body mass index (BMI), have also become more prevalent among childbearing women.^{10,15,24} Finally, progress in the prevention of preterm birth has been limited: the 2006 Institute of Medicine report on preterm birth and other reviews have concluded that the efforts for prevention have been largely unsuccessful.^{25,26}

In contrast to this general trend, however, recent studies from Finland and the Netherlands have reported decreasing rates of preterm birth for singleton births.^{24,27} Data on preterm birth rates from the Euro-Peristat project, a collaboration to monitor perinatal health in the European Union, also raise the question of whether rates are rising in all countries. Preterm birth rates in 2004 ranged from 5 to 11%, and it is possible that differences in trends over time explain some of this variation.¹ This study was thus designed to investigate time trends in preterm birth rates in the Euro-Peristat countries, and how these trends differ for singleton versus multiple pregnancies, as well as preterm deliveries with a spontaneous versus a non-spontaneous onset of labour.

Methods

Data

The scientific committee members of the countries participating in the Euro-Peristat II project (25 European member states and Norway) were invited to take part in this study.¹ Aggregate data from routine population-based sources were requested on number of births by gestational age (in completed weeks), by multiplicity, mode of delivery (vaginal or caesarean), and mode of onset of labour (caesarean section before labour, induction, or spontaneous), in 1996, 2000, 2004, and 2008. The definition of gestational age was the final estimate in the obstetrical records. We requested data on all live births, starting at 22 weeks of gestation. Stillbirths were excluded because registration criteria differ in routine sources across EU countries.²⁸

The time intervals were selected in order to allow comparisons with other Euro-Peristat data collected in 2000 and 2004. Countries that were unable to provide data for these years were asked to provide data from the closest available time point. If data were not available nationally, we requested population-based data from geographically defined regions. Appendix S1 describes data sources and geographical coverage.

Nineteen countries participated in the study. In Belgium, data came from Flanders, and in Germany, data came from three Länder. Data from the UK came from Scotland (gestational age was added to routine birth registers in Northern Ireland, England, and Wales in 2005 only). In France, data came from a routine nationally representative survey of all births. Spain and Portugal could only provide data by gestational age groups. The Czech Republic, the German Länder, Ireland, and Malta had no data from 1996. Malta and Sweden provided data from 2009 instead of 2008. Data from the French survey were available for 1995, 1998, 2003, and 2010. Most countries reported only minimal rates of missing data for gestational age, with the exception of Spain, where missing data were 11–19% depending on the period. Missing data were minimal for other variables. Missing data were excluded from analyses.

Austria, Ireland, Poland, Portugal, and Spain could not provide data on the onset of labour, and Slovakia only had this data for the last time point. Estonia, Lithuania, Malta, and Scotland collected data by whether the caesarean was planned/elective or an emergency. For these latter countries, planned caesarean sections were considered to occur before the onset of labour, although Estonia used data on the presence of labour to recode elective caesarean sections that followed the onset of labour.

Analysis

We computed preterm birth rates for all births and for singleton and multiple births for each time point. We also computed rates of multiple birth (multiple births/all births) and rates of spontaneous and non-spontaneous preterm birth separately, by multiplicity. We estimated risk ratios (RRs) of preterm birth with year as an independent continuous variable in each country separately for all births, and by subgroup, using log-binomial regression models.²⁹ Risk ratios were then transformed into percentage increases (risk ratio – 1) for presentation in graphs and tables. We used the exact time points available in each country. Random effects meta-analysis was used to test for heterogeneity in annual RRs across countries and to compute pooled measures. We also redid analyses after excluding births at 22–23 weeks of gestation because of concerns about cross-country differences in the recording of these infants, and confirmed that the results were similar. Correlations between country-level variables were assessed with Spear-

man's rank tests. Finally, we computed population-attributable risks to assess the contribution of multiple births to the overall preterm birth rate; confidence intervals were computed using Walter's limits.³⁰ Data were analysed using STATA 10.0 (StataCorp LP, College Station, TX, USA).

Results

Rates and trends in preterm birth

In 2008, preterm birth rates across Europe ranged from 5.5 to 11.1% for all live births, from 4.3 to 8.7% for singleton births, and from 42.2 to 77.8% for multiple births (Table 1). The annual percentage increases in preterm birth were significantly >0 in 13 out of the 19 countries included in the study for all live births (Figure 1). For singleton births, the percentage increases were positive for eight countries and negative in three countries. Thirteen countries experienced significant increases in preterm birth for multiple births, and no countries had significant decreases, although four countries had percentage changes <0 (Finland, the Netherlands, Sweden, and France). Meta-analysis found highly significant heterogeneity for all three measures using the Q-test; pooled RRs were over 1, but given the extensive heterogeneity between countries, they are of limited value (pooled measures: 0.7 (0.7–1.8), 0.2

(0.1–0.3), and 1.3 (1.2–1.4) for all, singleton, and multiple births, respectively). Country-level trends by year for multiples and singletons were not significantly associated, although the Spearman's correlation coefficient was positive ($\rho = 0.37$, $P = 0.12$).

Some countries experienced fluctuations in rates from one period to another, in particular for singletons. For instance, in Austria the rate increased over the period, but then declined slightly between 2004 and 2008. Furthermore, not all countries could provide data for all time points. We estimated annual trends for the period 2000–2008 in order to assess the sensitivity of our results to the selection of time points. Results were similar for all countries (Figure S1).

To test whether countries with lower initial rates of preterm birth experienced greater increases, we correlated preterm birth rates in the first time period with annual trends. The Spearman's correlation coefficients were negative, but the associations were not significant (all births, -0.266 , $P = 0.27$; singleton births, -0.244 , $P = 0.31$; and multiple births, -0.321 , $P = 0.18$).

Time trends in multiple births and population-attributable risks

Multiple births as a proportion of all live births ranged from 2.4 to 4.0% in 2008 (Table 2). Over the study period,

Table 1. Rates of preterm birth from 1996 to 2008 in 19 European countries

Country: region/ area	All live births					Singleton live births					Multiple live births				
	<i>n</i> (2008)	1996 %	2000 %	2004 %	2008 %	<i>n</i> (2008)	1996 %	2000 %	2004 %	2008 %	<i>n</i> (2008)	1996 %	2000 %	2004 %	2008 %
Austria	77 720	9.1	10.0	11.4	11.1	75 066	7.9	8.4	9.4	8.7	2654	58.2	67.5	74.6	77.8
Belgium: Flanders	69 187	7.0	7.8	8.1	8.0	66 672	5.2	6.0	6.3	6.2	2515	51.7	55.9	60.4	57.3
Czech Republic	119 455		5.4	7.7	8.3	114 722		4.2	6.0	6.3	4733		42.3	52.7	57.5
Estonia	16 031	5.5	5.9	5.9	6.2	15 506	4.9	5.1	4.9	4.6	525	38.5	46.2	47.6	51.0
Finland	59 486	5.8	6.1	5.6	5.5	57 767	4.5	4.7	4.4	4.3	1719	46.5	49.4	44.5	47.5
France*	14 696	5.4	6.2	6.3	6.6	14 261	4.5	4.7	5.0	5.5	435	40.5	48.2	44.3	42.1
Germany: 3 Länder	215 634		8.8	9.2	9.0	208 383		7.0	7.2	7.0	7251		61.7	61.8	64.2
Ireland	75 246		5.4	5.5	5.9	72 589		4.5	4.4	4.3	2657		41.8	42.3	49.9
Lithuania	31 287	5.3	5.3	5.3	5.9	30 510	4.5	4.6	4.5	4.7	777	41.3	42.6	42.7	49.4
Malta**	4152		6.0	7.2	6.7	4020		5.0	5.8	5.3	132		39.5	51.7	50.0
the Netherlands	175 160	7.8	7.7	7.4	7.4	168 829	6.2	6.0	5.7	5.7	6331	51.1	47.5	48.2	50.6
Norway	60 744	6.4	6.8	7.1	6.7	58 674	5.3	5.4	5.5	5.3	2070	43.4	43.9	49.2	48.3
Poland	414 480	6.8	6.3	6.8	6.6	404 452	6.1	5.5	5.8	5.5	10 028	43.1	44.0	50.2	51.2
Portugal	103 597	7.0	5.9	6.8	9.0	100 705	6.1	4.9	5.4	7.4	2892	45.9	49.6	54.9	63.5
Slovakia	53 624	5.1	5.4	6.3	6.8	52 227	4.4	4.5	5.2	5.6	1397	40.3	46.3	49.8	52.2
Slovenia	21 816	6.0	6.8	7.0	7.4	21 050	4.8	5.1	5.2	5.4	766	54.1	57.4	55.4	62.3
Spain	417 094	7.1	7.7	8.0	8.2	400 474	6.2	6.3	6.4	6.3	16 620	42.2	50.4	53.0	53.9
Sweden**	108 865	6.1	6.4	6.3	5.9	105 799	5.0	5.2	5.2	4.8	3066	44.1	43.4	45.2	43.3
UK: Scotland	58 275	7.0	7.4	7.6	7.7	56 423	5.8	6.1	6.3	6.1	1852	53.1	51.6	55.5	55.0

*Data from France come from a nationally representative sample of births, and the years are 1995, 1998, 2003, and 2010.

**2009, instead of 2008 data.

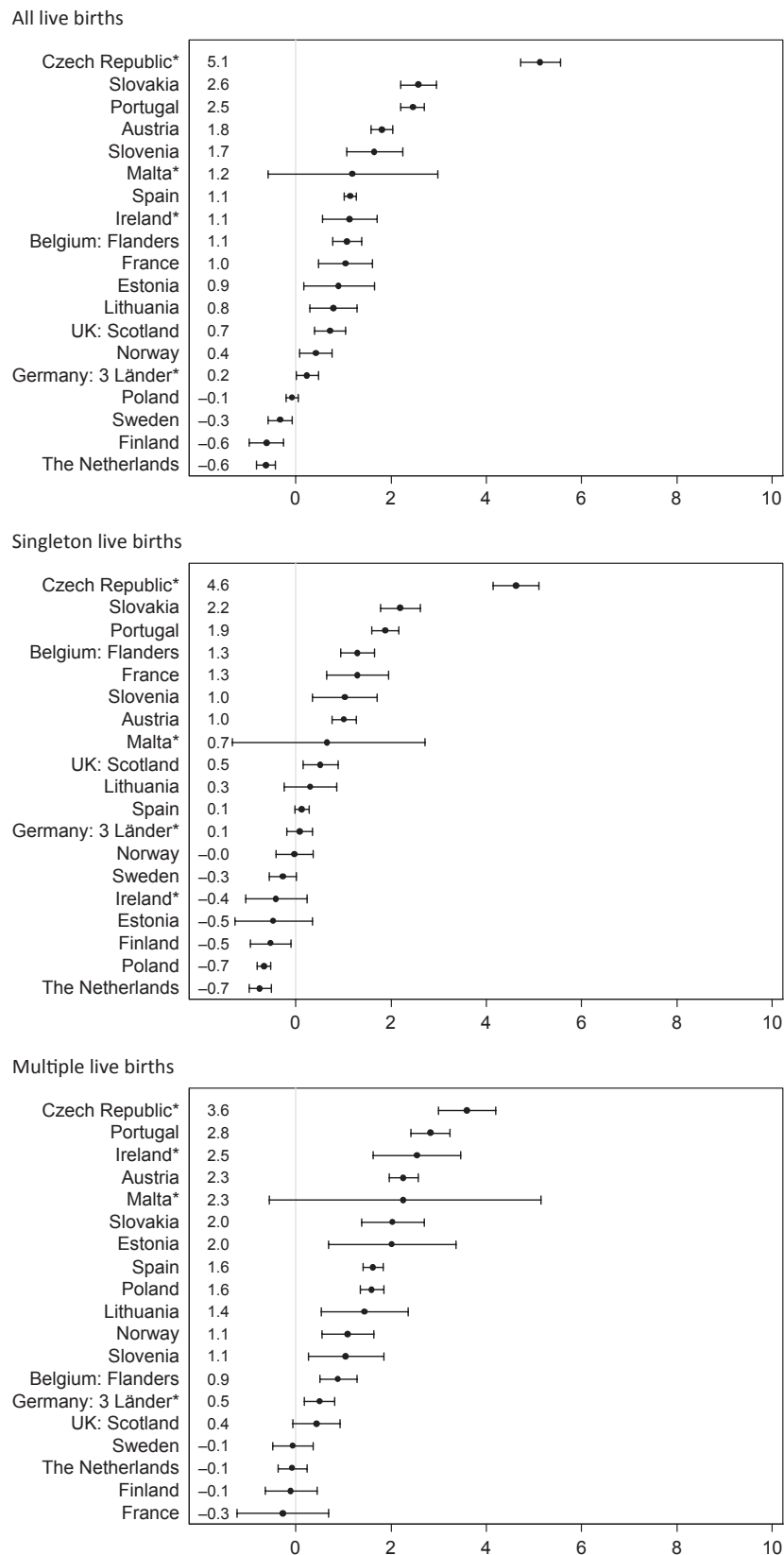


Figure 1. Average annual percentage change for preterm birth by country, 1996–2008.* Data series begins in 2000.

Table 2. Rates of multiple births per 100 live births, population-attributable risks, and average annual increases, 1996–2008

	Multiple birth rate 2008	Annual increase	Population-attributable risk 2008
Austria	3.4	3.2	21.3 (19.6–23.1)
Belgium: Flanders	3.6	−0.6*	23.2 (21.1–25.2)
Czech Republic	4.0	3.3*	24.5 (22.9–26.0)
Estonia	3.3	5.5*	24.7 (20.2–29.2)
Finland	2.9	−0.9*	22.5 (20.1–25.0)
France**	3.0	0.4	16.5 (11.6–21.4)
Germany: 3 Länder	3.4	0.3	21.5 (20.3–22.7)
Ireland	3.5	3.9*	27.2 (25.2–29.2)
Lithuania	2.5	1.8*	18.9 (15.3–22.6)
Malta***	3.2	0.8	21.1 (12.1–30.1)
the Netherlands	3.6	−0.3	22.1 (20.8–23.4)
Norway	3.5	1.2*	21.7 (19.4–24.0)
Poland	2.4	1.8*	16.8 (15.8–17.9)
Portugal	2.8	2.5*	17.4 (15.5–19.3)
Slovakia	2.7	2.7*	17.8 (15.0–20.5)
Slovenia	3.5	2.6*	26.9 (23.2–30.5)
Spain	3.8	3.2*	23.1 (22.3–24.0)
Sweden***	2.8	−0.6*	18.4 (16.5–20.2)
UK: Scotland	3.2	1.2*	20.2 (17.8–22.6)

*Confidence interval does not include 0.

**Data from France come from a nationally representative sample of births, and the years are 1995, 1998, 2003, and 2010.

***2009, instead of 2008 data.

this proportion was stable or decreasing in Belgium, Finland, the Netherlands, and Sweden, and increased steeply in Austria, the Czech Republic, Estonia, Ireland, and Spain. There was a significant association between the increase in the proportion of multiple births and the increase in preterm birth (Spearman's $\rho = 0.66$, $P = 0.021$). The proportion of the overall preterm birth rate attributable to multiples in 2008 ranged from about 17% in France, Poland, and Portugal, to 27% in Ireland and Slovenia.

Time trends by gestational age group

Figure 2 displays annual trends by gestational age group for singletons and multiples. Countries are ordered as in Figure 1. Although there was more variability in our estimates because of the smaller samples, this figure shows that increases in preterm birth were less marked for births at <32 weeks of gestation, in particular for multiples. Increases were not greatest for the 35–36 weeks of gestation group, and in many countries the largest proportional changes were observed between 32 and 34 weeks of gestation. Although many countries had similar trends for all gestational age groups, patterns could vary: the Netherlands experienced increases for singleton births at <32 weeks of gestation (0.9), but decreases for the two other groups (−

0.8 and −0.1). Divergent time trends are also observed in Poland, where decreases were larger for earlier preterm births. The group at 35–36 weeks of gestation represented a median of 60% of preterm births in participating countries (interquartile range, 57–62%; range, 55–66%).

Time trends in spontaneous and non-spontaneous preterm birth

For singletons, the rates of non-spontaneous preterm births ranged from 1.1 to 3.0% in 2008, whereas spontaneous onset births ranged from 2.8 to 4.8% (Table 3). For multiples, the rates of non-spontaneous preterm birth ranged from 12.0 to 34.4%, and spontaneous onset births from 15.1 to 38.2%. In each country, spontaneous preterm births were more frequent than non-spontaneous preterm births, with a few exceptions (Germany and Norway for singleton and multiple births, France and Malta for singleton births, and Belgium, Czech Republic, and Lithuania for multiple births).

Countries had differing time trends for non-spontaneous and spontaneous births for singleton births (Figure 3). In some countries both types of preterm birth increased (Belgium and Czech Republic), in others non-spontaneous preterm births increased, whereas spontaneous preterm births either remained unchanged or declined (France, Norway, and Sweden). Finally, some countries had increases in spontaneous preterm births with no change in non-spontaneous preterm births (Scotland and Germany). For multiples, in contrast, non-spontaneous preterm births increased in almost all countries. In Sweden and the Netherlands, where rates of multiple preterm births were stable, these increases were offset by the decline in spontaneous preterm births.

Discussion

Time trends in preterm births in Europe between 1996 and 2008 were highly heterogeneous, although the overall preterm birth rate and the multiple preterm birth rate increased in most countries. In contrast, singleton preterm birth rates were stable or decreased in about half of the countries in this analysis, challenging a widespread belief that rising rates have been the norm. In countries with rate increases, these were observed for all gestational age groups, not just the births closest to term.

Our study is limited by the data available from national systems: for instance, several countries did not have data for all the requested time points. We estimated annual trends using the available data points to compare across countries despite this limitation; a sensitivity analysis computing trends from 2000 to 2008 showed that our results were robust to the choice of period. Because our question was whether rates were rising, we tested for linear trends.

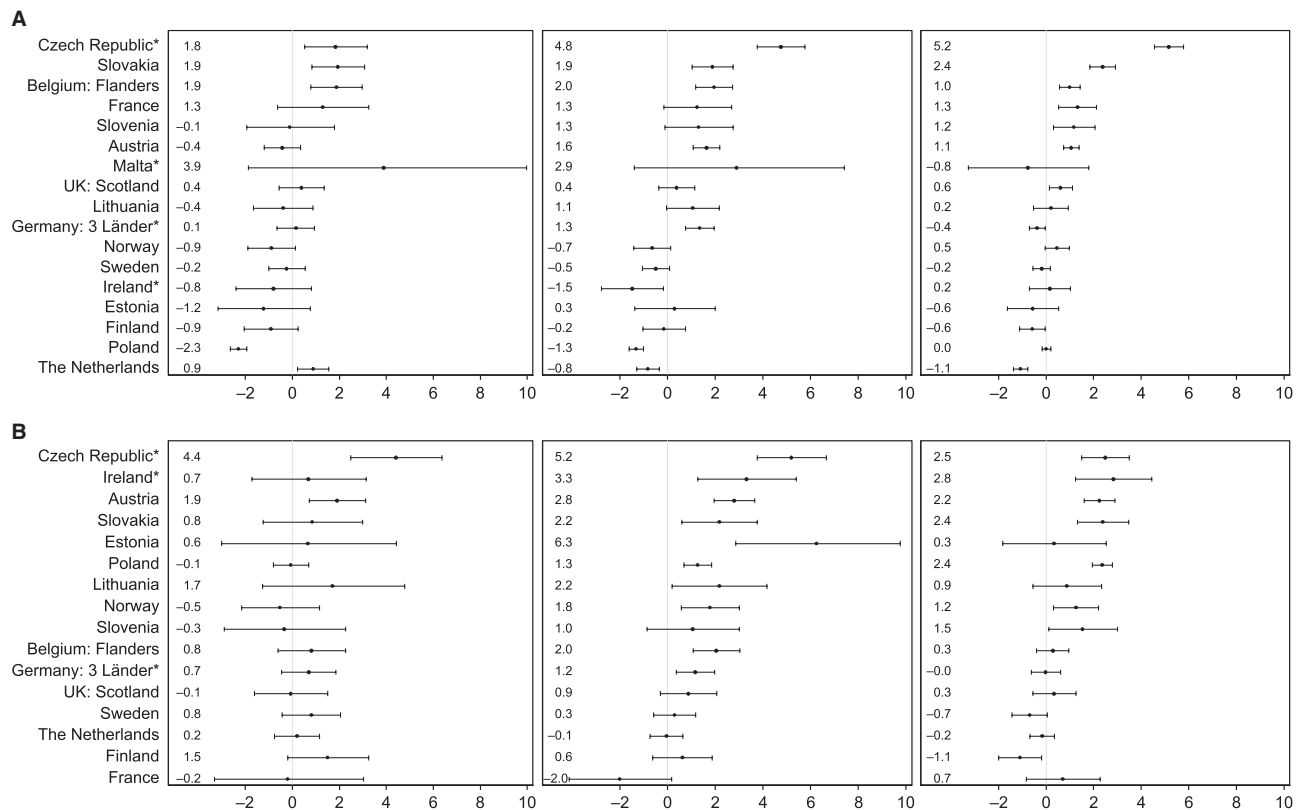


Figure 2. Average annual percentage change for birth at <32 weeks of gestation, 32–34 weeks of gestation, and 35–36 weeks of gestation among singleton live births (A), and among multiple live births (B), 1996–2008.

Rate fluctuations occurred in some countries, but no consistent patterns could be discerned, and we chose not to model these rises and falls.

Some countries could not provide data on the mode of the onset of labour, and among those that did, definitions differed ('elective' versus 'pre-labour' caesareans), although they were stable over the study period. Questions also exist about the measure of gestational age. We requested gestational age based on a common definition, the best obstetrical estimate, but we were unable to assess how clinicians assigned this estimate.³¹ Dating pregnancies using ultrasound shifts the gestational age distribution to the left, and can increase the preterm birth rate,³² but it can also decrease the rate by reducing errors in gestational age estimates.³¹ We cannot exclude the possibility that the rates of preterm birth were affected by an increased use of ultrasound for the dating of pregnancies over time, but in many European countries ultrasound dating was already widely used in the mid-1990s,^{11,13,27} and it is not clear whether this would lead to systematic upward or downward trends. A part of the wide variation in preterm birth rates across countries (5–11%) may result from differences in how gestational age is estimated; however, the fact that we observed substantial changes in the preterm birth rate over

the study period in some countries also confirms that large variations of this indicator are plausible.

More generally, it was not possible to assess the quality of data collection and case ascertainment; previous work in the Euro-Peristat group has found significant heterogeneity in routine data systems in Europe with respect to organisation and scope.³³ However, this study was restricted to population-based reporting systems with high coverage,³³ and used a pre-established protocol with common definitions developed collaboratively with participating data providers. This represents a strength over previous international studies that have relied on data in published reports and were unable to specify a priori definitions.¹⁶ Missing data on gestational age were low, with the exception of Spain, where civil registration data rely on parental reports,³⁴ and estimated trends in this case must be viewed with caution.

We requested data on live births instead of total births because of the differences in registration of stillbirths between European countries.^{28,33} Although it is important to consider the impact of stillbirths because many indicated preterm deliveries aim to reduce stillbirths, this exclusion is unlikely to affect our conclusions as preterm stillbirth is a rare outcome (about 2 per 1000 total births) compared

Table 3. Spontaneous and non-spontaneous preterm births per 100 live births by multiplicity from 1996 to 2008

Country: region/area	Singleton births								Multiple births							
	Spontaneous onset				Non-spontaneous onset				Spontaneous onset				Non-spontaneous onset			
	1996	2000	2004	2008	1996	2000	2004	2008	1996	2000	2004	2008	1996	2000	2004	2008
Austria																
Belgium: Flanders	3.8	3.9	4.3	4.2	1.5	2.1	2.1	2.0	29.0	33.0	33.4	30.6	22.7	22.9	27.0	26.7
Czech Republic		3.1	4.4	4.4		1.1	1.6	1.9		23.3	27.0	26.2		19.0	25.7	31.3
Estonia	3.4	3.9	3.8	3.6	1.4	1.1	1.1	1.1	29.9	30.2	30.5	33.5	8.7	16.0	17.1	17.5
Finland	3.3	3.7	3.5	3.2	1.1	1.0	0.9	1.1	30.7	35.9	29.0	31.9	15.8	13.5	15.5	15.5
France*	3.0	2.9	2.7	2.8	1.5	1.7	2.3	2.6	22.6	31.2	20.9	21.8	18.0	17.0	23.1	20.2
Germany: 3 Länder		3.8	4.0	4.0		3.0	3.1	3.0		27.4	27.8	32.0		32.3	33.1	32.1
Ireland																
Lithuania	3.0	3.1	3.1	3.2	1.5	1.5	1.4	1.5	23.0	23.0	23.9	15.1	18.3	19.5	18.5	34.4
Malta**		3.9	3.5	4.2		0.9	2.3	1.1		25.6	32.5	32.6		12.0	19.2	17.4
the Netherlands	4.4	4.4	4.2	3.9	1.7	1.6	1.5	1.8	34.3	32.1	32.8	29.9	15.9	15.4	15.4	20.7
Norway	3.2	3.3	3.1	3.1	1.6	2.1	2.3	2.1	24.5	24.5	25.6	25.3	14.7	19.0	23.1	21.6
Poland																
Portugal																
Slovakia				4.3				1.2				38.2				12.0
Slovenia	4.1	4.1	4.2	4.2	0.7	1.0	1.0	1.3	41.0	46.5	39.9	37.6	11.7	10.9	15.6	24.7
Spain																
Sweden**	3.2	3.3	3.4	3.1	1.6	1.7	1.7	1.7	27.4	28.5	28.1	25.0	16.6	13.9	16.5	17.9
UK: Scotland	4.5	4.8	5.0	4.8	1.3	1.2	1.2	1.3	39.9	36.3	36.9	36.3	13.2	15.3	18.6	18.8

*Data from France come from a nationally representative sample of births, and the years are 1995, 1998, 2003, and 2010.

**2009, instead of 2008 data.

with live preterm birth.¹ We set a common lower inclusion limit of 22 weeks of gestation for this study, and recomputed time trends after the exclusion of births under 24 weeks of gestation to verify that differences between countries in registration practices for live births at the limits of viability had no impact on our findings.

Our results show that the preterm birth rates for all births rose in many European countries, as was also found by the recent WHO study of preterm birth trends based on publicly available data in 64 countries in developed regions, Latin America, and the Caribbean.¹⁶ Our results add to this overview, however, by revealing that time trends can differ substantially between the overall preterm birth rate and the singleton preterm birth rate, that trends were similar across gestational age groups, and by documenting changes in multiple births rates over time and their contribution to the overall preterm rates.

We found a strong correlation between increases in multiple births and preterm birth, corroborating previous studies.¹⁸ Policies related to the use of assisted reproductive technology (ART) are highly variable in Europe, and these affect the multiple birth rate resulting from ART.¹⁷ For instance, national elective single embryo transfer (eSET) policies have been adopted by several countries, including

Belgium and Sweden.³⁵ eSET has also been extensively promoted in Finland, despite the fact that it is not mandatory nor an official policy.³⁶ In contrast, other European countries have no such policies: in Italy, the law requires the transfer of all fertilised embryos in each cycle, although it limits the number of fertilised embryos to three.³⁷ Data collected by the European Society of Human Reproduction and Embryology (ESHRE) from IVF centres documents wide differences in the rates of single embryo transfer across Europe (from 10 to ~70%)¹⁷; countries in our analysis with negative trends in their preterm birth rates, such as Belgium, Finland, and Sweden, had a high proportion of eSET (50.4, 62.1, and 69.5%, respectively). In contrast, countries with increases in their multiple birth rate had a lower proportion of single embryo transfers (Austria, 22.6%; Ireland, 19.1; and Portugal, 19.0).

Multiple births also affected the overall preterm birth rate because of increases in the preterm birth rate among multiples. For multiple births, and with the data on mode of onset of labour included in the analysis, non-spontaneous preterm birth rates increased in almost all countries. In almost all countries with data on mode of onset of labour, non-spontaneous preterm birth rates increased. Overall, our data showed that the population-attributable risk asso-

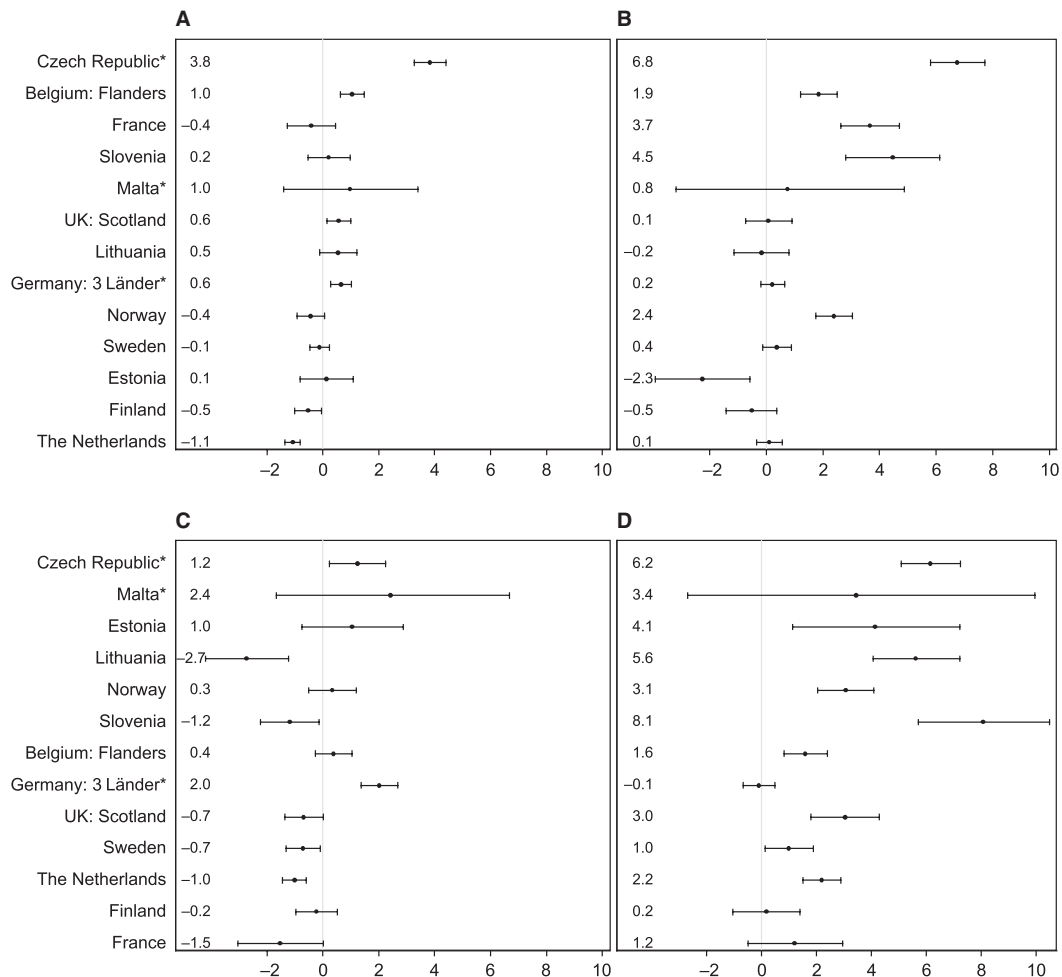


Figure 3. Average annual percentage change for spontaneous (A) and non-spontaneous (B) preterm births among singleton live births, and annual rate ratios for spontaneous (C) and non-spontaneous (D) preterm births among multiple live births, 1996–2008.

ciated with multiple pregnancies was substantial, ranging from 17 to 27%.

We found that many countries had unchanging or declining singleton preterm birth rates, as also shown by studies from Finland and the Netherlands over different time periods,^{24,27} while elsewhere preterm birth rates rose considerably. We found increases in non-spontaneous preterm births in some countries, corroborating other studies concluding that these births were a driving force behind rising preterm birth rates.^{13,15,22,38} However, we observed extensive heterogeneity in the proportions of preterm births by mode of onset of labour, and in the evolution of non-spontaneous preterm births over time. A consistent pattern of rising preterm birth rates driven primarily by non-spontaneous preterm births was not detected.

We also showed that spontaneous preterm births played a role in determining overall trends, as reported in other in-depth studies of preterm birth in Denmark, Scotland,

Australia, Finland, and the Netherlands.^{11,13,15,24,27} Rates of spontaneous preterm births rose in some countries, and where overall preterm birth rates decreased, these trends affected spontaneous preterm births. The reasons for trends in the spontaneous preterm birth rate are poorly understood, and countries with similar populations have experienced divergent trends, as in Denmark and Finland, for instance.^{11,24} Researchers have proposed a range of factors that could contribute to varying preterm birth rates between populations, including older maternal age, obesity, higher-risk migrant populations, smoking during pregnancy, use of IVF, diabetes, *Chlamydia trachomatis* infection, and previous induced abortions, but their relative contribution remains to be established.^{11,13,15,24,27} Obstetric practices related to the management of preterm birth risk (screening for short cervix, use of progesterone, and prescription of bed rest, for instance) may differ across countries; however, we are not aware of any studies that have

assessed variations in these practices across countries and their impact on national preterm birth rates. The prevalence of work leaves for pregnant women differ in Europe, and this may reduce the impact of work-related risk factors on preterm birth.³⁹ Economic factors may also play a role: some studies find that preterm birth rates have risen more steeply among women of lower socio-economic status.⁹ Comparative cross-national studies provide an opportunity to test these multiple hypotheses; the Euro-Peristat network as well as birth cohorts that have been established in Europe are promising platforms for future research in this area.

Although annual changes in the rate of preterm birth were modest in most countries, the impact is substantial when assessed in terms of the numbers of preterm infants. If every country had experienced trends similar to Finland or the Netherlands over the study period (−0.6% per year), over 24 000 fewer preterm babies would have been born in 2008, or 1.2% of the over two million births in the participating countries. Evaluating the health impact of rising rates is more complex than computing the number of ‘excess’ preterm infants, however. Several studies have suggested that rises in the rate of indicated preterm births may be associated with better perinatal outcomes. For twins, more intensive prenatal care was related to higher rates of preterm birth, and mothers receiving more intensive care had lower neonatal mortality.⁴⁰ For singletons, mortality rates were observed to decline more steeply among non-spontaneous than spontaneous preterm births.⁴¹ On the other hand, there is a growing body of research documenting the adverse short- and longer-term health consequences of being born preterm, even at later gestational ages.^{6,8} The large variability in the proportions of non-spontaneous preterm births suggests that there are contrasting interpretations of the current evidence base related to the positive and negative consequences of inducing a delivery before term.

Conclusion

Time trends in the rates of preterm birth since the mid-1990s show a striking diversity in 19 European countries. For multiples, rates have generally increased, although the range is wide; for singletons, however, the direction of change differs. These results call for further examination of reproductive and perinatal health policies and medical practices in European countries, and for an assessment of their impact on the population risk of preterm birth. To enable comparative analyses, data on preterm birth need to be included in international health databases.

Disclosure of interests

The authors have no conflicts of interest or disclosures to declare.

Contribution to authorship

JZ, BB, and KS conceived the study, ND carried out statistical analysis, ADM, JC, LS, LI, MG, and MG contributed to the interpretation of the results and revised successive versions of the article. Members of the Euro-Peristat preterm birth group were responsible for the provision, accuracy, and interpretation of data in their country: they commented on initial and final versions of the article. All authors approved the final article.

Details of ethics approval

This article is based on the analysis of aggregate data provided from routine data sources, and is exempt from ethical approvals at INSERM in France. The transmission of data was consistent with existing authorisations for each routine data source in terms of the allowable minimum cell sizes.

Funding

This analysis was partially funded by a grant to the Euro-Peristat project from the European Commission (2010 13 01). JZ also received funding from the European Commission, Research Directorate, Marie Curie, IOF Fellowship, grant no. 254171. The funding agency was not involved in the study.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Annual percentage changes of preterm birth by year, 2000–2008.

Appendix S1. Data sources. ■

References

- 1 EURO-PERISTAT project in collaboration with SCPE, EUROCAT and EURONEOSTAT. Better statistics for better health for pregnant women and their babies in 2004. European Perinatal Health Report 2008. Available at www.europeristat.com, 2008.
- 2 Larroque B, Ancel PY, Marret S, Marchand L, Andre M, Arnaud C, et al. Neurodevelopmental disabilities and special care of 5-year-old children born before 33 weeks of gestation (the EPIPAGE study): a longitudinal cohort study. *Lancet* 2008;371:813–20.
- 3 Zeitlin J, Draper ES, Kollee L, Milligan D, Boerch K, Agostino R, et al. Differences in rates and short-term outcome of live births before 32 weeks of gestation in Europe in 2003: results from the MOSAIC cohort. *Pediatrics* 2008;121:e936–44.
- 4 Kramer MS, Demissie K, Yang H, Platt RW, Sauve R, Liston R. The contribution of mild and moderate preterm birth to infant mortality. Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. *JAMA* 2000;284:843–9.
- 5 Gouyon JB, Vintejoux A, Sagot P, Burguet A, Quantin C, Ferdynus C. Neonatal outcome associated with singleton birth at 34–41 weeks of gestation. *Int J Epidemiol* 2010;39:769–76.
- 6 Boyle EM, Poulsen G, Field DJ, Kurinczuk JJ, Wolke D, Alfirevic Z, et al. Effects of gestational age at birth on health outcomes at 3 and 5 years of age: population based cohort study. *BMJ* 2012;344:e896.

- 7 Crump C, Sundquist K, Sundquist J, Winkleby MA. Gestational age at birth and mortality in young adulthood. *JAMA* 2011;306:1233–40.
- 8 Crump C, Sundquist K, Winkleby MA, Sundquist J. Early-term birth (37–38 weeks) and mortality in young adulthood. *Epidemiology* 2013;24:270–6.
- 9 Auger N, Gamache P, Adam-Smith J, Harper S. Relative and absolute disparities in preterm birth related to neighborhood education. *Ann Epidemiol* 2011;21:481–8.
- 10 Keirse MJ, Hanssens M, Devlieger H. Trends in preterm births in Flanders, Belgium, from 1991 to 2002. *Paediatr Perinat Epidemiol* 2009;23:522–32.
- 11 Langhoff-Roos J, Kesmodel U, Jacobsson B, Rasmussen S, Vogel I. Spontaneous preterm delivery in primiparous women at low risk in Denmark: population based study. *BMJ* 2006;332:937–9.
- 12 Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S, et al. Births: final data for 2005. *Natl Vital Stat Rep* 2007;56:1–103.
- 13 Norman JE, Morris C, Chalmers J. The effect of changing patterns of obstetric care in Scotland (1980–2004) on rates of preterm birth and its neonatal consequences: perinatal database study. *PLoS Med* 2009;6:e1000153.
- 14 Ooki S. The effect of an increase in the rate of multiple births on low-birth-weight and preterm deliveries during 1975–2008. *J Epidemiol* 2010;20:480–8.
- 15 Tracy SK, Tracy MB, Dean J, Laws P, Sullivan E. Spontaneous preterm birth of liveborn infants in women at low risk in Australia over 10 years: a population-based study. *BJOG* 2007;114:731–5.
- 16 Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet* 2012;379:2162–72.
- 17 de Mouzon J, Goossens V, Bhattacharya S, Castilla JA, Ferraretti AP, Korsak V, et al. Assisted reproductive technology in Europe, 2007: results generated from European registers by ESHRE. *Hum Reprod* 2012;27:954–66.
- 18 Blondel B, Kogan MD, Alexander GR, Dattani N, Kramer MS, Macfarlane A, et al. The impact of the increasing number of multiple births on the rates of preterm birth and low birthweight: an international study. *Am J Public Health* 2002;92:1323–30.
- 19 Blondel B, Macfarlane A, Gissler M, Breart G, Zeitlin J. Preterm birth and multiple pregnancy in European countries participating in the PERISTAT project. *BJOG* 2006;113:528–35.
- 20 Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet* 2008;371:261–9.
- 21 Goldenberg RL, Gravett MG, Iams J, Papageorgiou AT, Waller SA, Kramer M, et al. The preterm birth syndrome: issues to consider in creating a classification system. *Am J Obstet Gynecol* 2012;206:113–8.
- 22 Zhang X, Kramer M. The rise in singleton preterm births in the USA: the impact of labour induction. *BJOG* 2012;119:1309–15.
- 23 MacDorman MF, Declercq E, Zhang J. Obstetrical intervention and the singleton preterm birth rate in the United States from 1991–2006. *Am J Public Health* 2010;100:2241–7.
- 24 Jakobsson M, Gissler M, Paavonen J, Tapper AM. The incidence of preterm deliveries decreases in Finland. *BJOG* 2008;115:38–43.
- 25 Iams JD, Romero R, Culhane JF, Goldenberg RL. Primary, secondary, and tertiary interventions to reduce the morbidity and mortality of preterm birth. *Lancet* 2008;371:164–75.
- 26 Behrman RE, Butler AS, editors. *Preterm Birth: Causes, Consequences, and Prevention*. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes. Washington (DC): The National Academies Press (US), 2007.
- 27 Schaaf JM, Mol BW, Abu-Hanna A, Ravelli AC. Trends in preterm birth: singleton and multiple pregnancies in the Netherlands, 2000–2007. *BJOG* 2011;118:1196–204.
- 28 Mohangoo AD, Buitendijk SE, Szamotulska K, Chalmers J, Irgens LM, Bolumar F, et al. Gestational age patterns of fetal and neonatal mortality in Europe: results from the Euro-Peristat project. *PLoS ONE* 2011;6:e24727.
- 29 Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol* 2005;162:199–200.
- 30 Walter SD. Calculation of attributable risks from epidemiological data. *Int J Epidemiol* 1978;7:175–82.
- 31 Wingate MS, Alexander GR, Buekens P, Vahratian A. Comparison of gestational age classifications: date of last menstrual period vs. clinical estimate. *Ann Epidemiol* 2007;17:425–30.
- 32 Blondel B, Morin I, Platt RW, Kramer MS, Usher R, Breart G. Algorithms for combining menstrual and ultrasound estimates of gestational age: consequences for rates of preterm and postterm birth. *BJOG* 2002;109:718–20.
- 33 Gissler M, Mohangoo AD, Blondel B, Chalmers J, Macfarlane A, Gaizauskiene A, et al. Perinatal health monitoring in Europe: results from the EURO-PERISTAT project. *Inform Health Soc Care* 2010;35:64–79.
- 34 Juarez S, Alonso Ortiz T, Ramiro-Farinas D, Bolumar F. The quality of vital statistics for studying perinatal health: the Spanish case. *Paediatr Perinat Epidemiol* 2012;26:310–5.
- 35 Cook JL, Collins J, Buckett W, Racowsky C, Hughes E, Jarvi K. Assisted reproductive technology-related multiple births: Canada in an international context. *J Obstet Gynaecol Can* 2011;33:159–67.
- 36 Tiitinen A, Gissler M. Effect of in vitro fertilization practices on multiple pregnancy rates in Finland. *Fertil Steril* 2004;82:1689–90.
- 37 La Sala GB, Nicoli A, Villani MT, Rondini I, Moscato L, Blickstein I. The 2004 Italian legislation on the application of assisted reproductive technology: epilogue. *Eur J Obstet Gynecol Reprod Biol* 2012;161:187–9.
- 38 Ananth CV, Joseph KS, Oyelese Y, Demissie K, Vintzileos AM. Trends in preterm birth and perinatal mortality among singletons: United States, 1989 through 2000. *Obstet Gynecol* 2005;105(5 Pt 1):1084–91.
- 39 Saurel-Cubizolles MJ, Zeitlin J, Lelong N, Papiernik E, Di Renzo GC, Breart G. Employment, working conditions, and preterm birth: results from the Europop case-control survey. *J Epidemiol Community Health* 2004;58:395–401.
- 40 Kogan MD, Alexander GR, Kotelchuck M, MacDorman MF, Buekens P, Martin JA, et al. Trends in twin birth outcomes and prenatal care utilization in the United States, 1981–1997. *JAMA* 2000;284:335–41.
- 41 Lisonkova S, Hutcheon JA, Joseph KS. Temporal trends in neonatal outcomes following iatrogenic preterm delivery. *BMC Pregnancy Childbirth* 2011;11:39.